

Investigating the most appropriate dose and effectiveness of thiotepa in combination with ifosphamide, etoposide and rituximab in patients with lymphoma arising in the brain or spinal cord

Submission date 03/12/2014	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 03/12/2014	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/02/2023	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-chemotherapy-and-biological-therapy-for-lymphoma-of-the-brain-or-spinal-cord-tier>

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

2014-000227-24

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

17668

Study information

Scientific Title

A study of thiotepa, ifosphamide, etoposide and rituximab for the treatment of relapsed or refractory primary central nervous system lymphoma

Acronym

TIER

Study objectives

The phase I dose finding component is a 3+3 cohort design which will recruit up to 18 patients in order to find the MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). All patients recruited into phase I at the MTD will also contribute towards phase II. The phase II study is based on an A'Hern's design to assess the activity of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). 28 patients will be recruited in total in phase II (including some patients from phase I).

Ethics approval required

Old ethics approval format

Ethics approval(s)

14/LO/1568; First MREC approval date

Study design

Non-randomised, interventional

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Primary central nervous system lymphoma

Interventions

Etoposide, 250mg/m² day 2 of 21 day cycle; Ifosphamide, 2g/m²/day days 2-4 for each 21 day cycle.; Rituximab, 375mg/m²/day days 1-2 for each 21 day cycle; Thiotepa, Chemotherapy (doses 20mg/m² - 50mg/m²)

Intervention Type

Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

1. Etoposide 2. Ifosphamide 3. Rituximab 4. Thiotepa

Primary outcome(s)

MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER)

Timepoint(s): End of 2 cycles of treatment

Key secondary outcome(s)

1. 2 year event free survival (EFS); Timepoint(s): 2 years after trial treatment
2. 2 year overall survival (OS); Timepoint(s): 2 years after trial treatment
3. 2 year progression free survival (PFS); Timepoint(s): 2 years after trial treatment
4. CR rate after 2 cycles of TIER; Timepoint(s): End of 2 cycles of treatment
5. Overall response rate (Complete Response (CR) + Complete Response: unconfirmed (CRu) + Partial Res; Timepoint(s): end of 2 cycles of treatment
6. Proportion of patients proceeding to high-dose therapy and autologous stem cell transplant (HDT-AS; Timepoint(s): Following trial treatment
7. Rate of successful stem cell harvest; Timepoint(s): After completing trial treatment
8. Toxicity of TIER using the National Cancer Institute Common Terminology Criteria for Adverse Event; Timepoint(s): All cycles of trial treatment

Completion date

31/10/2021

Eligibility

Key inclusion criteria

- 1 Age \geq 16 years of age
2. Histologically confirmed* CD20+ Diffuse Large B Cell Lymphoma (DLBCL) confined to the central nervous system
3. Relapsed or refractory primary central nervous system lymphoma (PCNSL) according to the following definition :
 - 3.1. One or two prior chemotherapy regimen(s), of which at least one regimen contained highdose methotrexate at a dose of $>1\text{g/m}^2$.
 - 3.2. Minimum of one cycle containing highdose methotrexate
4. ECOG performance status 0,1 or 2 (or 3 if attributed to lymphoma)
5. Adequate organ function:
 - 5.1. Bone marrow: platelets $>80 \times 10^9/\text{L}$, neutrophils $>1 \times 10^9/\text{L}$, haemoglobin $>80 \text{ g/L}$
 - 5.2. Hepatic: bilirubin $<1.5 \times$ upper limit of normal (ULN) (unless isolated unconjugated hyperbilirubinaemia attributable to Gilbert's syndrome)
 - 5.3. Renal: eGFR $\geq 40\text{ml/min}$ (Cockcroft-Gault)
 - 5.4. Cardiorespiratory (as judged by the Local Investigator): clinically relevant cardiac or pulmonary function tests must be performed if there is a previous history of significant cardiac or pulmonary impairment
6. Able to comply with the scanning requirements of the study
7. Valid Informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Total final enrolment

36

Key exclusion criteria

1. Systemic involvement with lymphoma
2. Active infection requiring intravenous antimicrobials
3. Chemotherapy for lymphoma within 4 weeks registration
4. Wholebrain radiotherapy within 6 months of registration
5. Relapse within 1 year of a Thiotepabased autologous stem cell transplant
6. Prior therapy with the RIE (Rituximab – ifosphamide and etoposide) regimen
7. Evidence of HIV or Hepatitis C infection
8. Hepatitis B infection*
9. Serum albumin <25g/l
10. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry)
11. Competent pPatients and competent patients with partners of childbearing potential not willing to use effective contraception during and for 12 months after therapy

Date of first enrolment

12/12/2014

Date of final enrolment

30/04/2019

Locations**Countries of recruitment**

United Kingdom

England

Scotland

Study participating centre

Cancer Research UK Clinical Trials Unit

School of Cancer Sciences

University of Birmingham

Edgbaston

Birmingham

United Kingdom
B15 2TT

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Aberdeen Royal Infirmary
Aberdeen
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AB25 2ZN

Study participating centre
Beatson West of Scotland Cancer Centre
Glasgow
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G12 0YN

Study participating centre
King's College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
St James University Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
Aintree University Hospital
Liverpool
United Kingdom
L9 7AL

Study participating centre
The Christie
Manchester
United Kingdom
M20 4BX

Study participating centre
Freeman Hospital
Newcastle
United Kingdom
NE7 7DN

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Derriford Hospital
Plymouth
United Kingdom
PL6 8DH

Study participating centre
University College Hospital
London
United Kingdom
NW1 2BU

Study participating centre
The Royal Marsden Hospital
Sutton
United Kingdom
SM2 5PT

Study participating centre
Royal Hallamshire Hospital
Sheffield
United Kingdom
S10 2JF

Study participating centre
Southampton General Hospital
Southampton
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SO16 6YD

Study participating centre
New Cross Hospital
Wolverhampton
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WV10 0QP

Sponsor information

Organisation
University of Birmingham

ROR
<https://ror.org/03angcq70>

Funder(s)

Funder type
Government

Funder Name

Leukaemia and Lymphoma Research

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Participant information sheet	26/10/2021	15/02/2023	Yes	No
Basic results		15/02/2023	15/02/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet		11/11/2025	11/11/2025	No	Yes
Plain English results			25/10/2022	No	Yes